UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,300	05/11/2001	Gregory Ford	STAN177	7800

24353 7590 11/05/2002

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/854,300	Applicant(s) FORD ET AL.
	Examiner " Neon" Phuong Huynh	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *11-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7& 11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-19 are pending.

2. Applicant's election of Group II, claims 1-10 drawn to a nucleic acid encoding Grail protein of SEQ ID NO: 7, expression cassette, cell comprising said cassette and method of producing Grail protein, filed 8/12, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 11-19 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-10, drawn to a nucleic acid encoding Grail protein of SEQ ID NO: 7, expression cassette, cell comprising said cassette and method of producing Grail protein are being acted upon in this Office Action.

5. Applicant should amend the first line of the specification to reflect the relationship between the instant application and 60/203,513 filed 5/11/00 as stated on the oath.

6. The disclosure is objected to because of the following **informalities**: (1) the "5□ and 3□" on page 7, paragraphs 26, 28 should have been 5' and 3'. (2) The symbols "□" on page 13 paragraphs 50-51 should be corrected. Appropriate action is required.

7. Claims 1-10 are objected to because they drawn to non-elected polynucleotide of SEQ ID NO: 5. Further, SEQ ID NO: 7 is a polynucleotide and not a polypeptide as indicated in the field <212> of the sequence listing.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence of SEQ ID NO: 7 encoding a GRAIL protein of SEQ ID NO: 8 for screening T cell anergy in vitro, (2) an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence of SEQ ID NO: 7 encoding a GRAIL protein wherein said GRAIL protein comprises the amino acid sequence as set forth in SEQ I DNO: 8, (3) an expression cassette comprising the isolated nucleic acid other than a naturally occurring chromosome comprising a sequence of SEQ ID NO: 7 encoding a GRAIL protein of SEQ ID NO: 8 operatively linked to transcriptional and translational control sequence for the expression of said GRAIL protein, (4) a host cell comprising the expression cassette mentioned above and the cellular progeny of said host cell, (5) a host cell comprising an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence of SEQ ID NO: 7 encoding a GRAIL protein of SEQ ID NO: 8 and the cellular progeny of said host cell, and (6) a method for producing GRAIL protein, said method comprising growth a host cell comprising the expression cassette mentioned above and the cellular progeny of said host cell whereby said GRAIL protein is expressed, and isolating said GRAIL protein free of other proteins, **does not** reasonably provide enablement for (1) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence encoding *any* GRAIL protein", (2) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* GRAIL protein wherein said GRAIL protein comprises the amino acid sequence set forth in "SEQ ID NO: 7", (3) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* GRAIL protein wherein said GRAIL protein "comprises" *any* SEQ ID NO: 7 "fragment thereof", (4) *any* isolated nucleic acid "comprising" at least 18 or 50 contiguous nucleotides of SEQ ID NO: 7, (5) *any* isolated nucleic acid that hybridizes under "stringent conditions" to the nucleic acid sequence of SEQ ID NO: 7, (6) *any* expression cassette comprising *any* "transcriptional initiation region" functional in *any* expression host, *any* nucleic acid having *any* sequence of *any* isolated nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* "GRAIL protein" under the transcriptional regulation of said transcriptional initiation region and a transcriptional termination region functional in said expression host (7) *any* cell comprising any expression cassette mentioned above as part of *any* extrachromosomal element or integrated into the genome of a host cell as a result of introduction of said expression cassette into said host cell and the cellular progeny of

said host cell, (8) *any* cell comprising *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence" encoding *any* "GRAIL protein" as part of an extrachromsomal element or integrated into the genome of a host cell as a result of introduction of said expression cassette into said host cell, and the cellular progeny of said host cell, and (9) a method of producing *any* "GRAIL protein", said method comprising growing cell comprising the expression cassette comprising transcriptional initiation region functional in expression host, *any* nucleic acid having *any* sequence comprising *any* isolated nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence encoding *any* GRAIL protein", whereby said GRAIL protein is expressed and isolating said GRAIL protein free of other proteins for diagnosis of T cell anergy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only five isolated nucleic acid sequences comprising SEQ ID NO: 1 which encodes MRC-OX44 (reference 9.3.1-2), SEQ ID NO: 2 which encodes Nurr2 (reference 19.9.6-3), SEQ ID NO: 3 which encodes lymphtactin (reference 6.5.2-4), SEQ ID NO: 4 which encodes cbl-b (reference A9.5.7-4), SEQ ID NO: 5 which encodes the murine GRAIL of SEQ ID NO: 6 (reference 1-4) and SEQ ID NO: 7 which encodes the human GRAIL of SEQ ID NO: 8 for producing said GRAIL protein. The GRAIL protein is approximately 50kD and migrates as a 3.75K mRNA on Northern. The specification further discloses the polynucleotide encoding GRAIL is used for expressing the GRAIL protein for identifying or detecting the expression of GRAIL in a biological specimen associated with T cell angery in vitro.

The specification does not teach how to make and use *any* "nucleic acid molecule" mentioned above for producing *any* "GRAIL protein" because the term "nucleic acid molecule" without specific SEQ ID NO has no structure associated with said term much less about the

function of *any* "GRAIL protein". Further, the specification does not defines "GRAIL protein". Given the indefinite number of undisclosed "nucleic acid molecule", it is unpredictable which undisclosed "nucleic acid molecule" would encode "GRAIL protein", in turn, would be useful for screening T cell anergy.

With regard to claim 2, SEQ ID NO: 7 is an isolated nucleic molecule encoding GRAIL protein comprising the amino acid sequence of SEQ ID NO 8.

With regard to claims 3-5, the term "comprising" is open ended. It expands the "fragment" of SEQ ID NO: 7 such as 18 or 50 contiguous nucleotides to include additional nucleotides at either or both ends. There is insufficient guidance as to the additional nucleotides encoding the corresponding polypeptide and whether the resulting polynucleotide after additional nucleotide would maintain both structure and function as the claimed polynucleotide of SEQ ID NO: 7. Further, there is insufficient working example demonstrating that adding additional nucleotide to the fragment of SEQ ID NO: 7 would encode the same protein, much less maintain the structure and function of the protein, in turn, would be useful for detecting T cell anergy. Given the lack of guidance as to which changes can be tolerated and relates to its functional usefulness, there is no expectation of success, let alone predicting which undisclosed nucleotide would be useful for screening T cell anergy.

Attwood *et al*. teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (See figure, entire document). It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama *et al* teach that the human glycosylation-inhibiting factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (Figure 1 in particular). Yet, Mikayama *et al.* teach further that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF bioactivity (Abstract in particular). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet *et al* teach that a single Glu to Val substitution in the subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia

and blood flow blockages (pages 126-128, section 6-3A and page 230, paragraph bridging columns in particular).

With regard to isolated nucleic acid that hybridizing under "stringent conditions" as recited in claim 6, the claim encompasses any random nucleotide sequence of any length which hybridizes under undisclosed "stringent conditions" that may or may not bind specifically to SEQ ID NO: 7 which encodes a "GRAIL protein". Given the indefinite numbers of oligonucleotide and the undisclosed hybridization conditions for the specific polynucleotide, the lack of guidance and insufficient number of working examples, it is unpredictable which undisclosed oligonucleotides would hybridize specifically to the nucleotide of SEQ ID NO: 7, in turn, would be useful for screening T cell anergy.

The state of the prior art as exemplified by Wallace *et al* and Sambrook *et al* is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable. Even if the probe is a 20mer, the total number of hits in a database search was 143,797,728, which suggest that some of the nucleotide fragment encompassed by the claim would not preferentially hybridize to the nucleic acid sequence of SEQ I DNO: 7 that encodes a GRAIL protein. Further, since the hybridization condition for the particular nucleotide is not specific, it follows that the method for screening for T cell anergy is not enable.

With regard to claims 7-10, since the isolated nucleic acid in claim 1 is not enabled, it follows that the expression cassette comprising the undisclosed nucleic acid encoding *any* GRAIL protein under the transcriptional regulation, transcriptional initiation and termination is not enabled. It also follows that the host cell comprising said expression cassette is not enabled, in turn, the method making the protein such as GRAIL is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

10. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence encoding *any* GRAIL protein", (2) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* GRAIL protein wherein said GRAIL protein comprises the amino acid sequence set forth in "SEQ ID NO: 7", (3) *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* GRAIL protein wherein said GRAIL protein "comprises" *any* SEQ ID NO: 7 "fragment thereof", (4) *any* isolated nucleic acid "comprising" at least 18 or 50 contiguous nucleotides of SEQ ID NO: 7, (5) *any* isolated nucleic acid that hybridizes under "stringent conditions" to the nucleic acid sequence of SEQ ID NO: 7, (6) *any* expression cassette comprising *any* "transcriptional initiation region" functional in *any* expression host, *any* nucleic acid having *any* sequence of *any* isolated nucleic acid molecule other than a naturally occurring chromosome comprising *any* sequence encoding *any* "GRAIL protein" under the transcriptional regulation of said transcriptional initiation region and a transcriptional termination region functional in said expression host (7) *any* cell comprising any expression cassette mentioned above as part of *any* extrachromosomal element or integrated into the genome of a host cell as a result of introduction of said expression cassette into said host cell and the cellular progeny of said host cell, (8) *any* cell comprising *any* nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence" encoding *any* "GRAIL protein" as part of an extrachromosomal element or integrated into the genome of a host cell as a result of introduction of said expression cassette into said host cell, and the cellular progeny of said host cell, and (9) a method of producing *any* "GRAIL protein", said method comprising growing cell comprising the expression cassette comprising transcriptional initiation region functional in expression host, *any* nucleic acid having *any* sequence comprising *any* isolated nucleic acid molecule other than a naturally occurring chromosome comprising *any* "sequence encoding *any* GRAIL protein", whereby said GRAIL protein is expressed and isolating said GRAIL protein free of other proteins for diagnosis of T cell anergy.

The specification discloses only five isolated nucleic acid sequences comprising SEQ ID NO: 1 which encodes MRC-OX44 (reference 9.3.1-2), SEQ ID NO: 2 which encodes Nurr2

(reference 19.9.6-3), SEQ ID NO: 3 which encodes lymphtactin (reference 6.5.2-4), SEQ ID NO: 4 which encodes cbl-b (reference A9.5.7-4), SEQ ID NO: 5 which encodes the murine GRAIL of SEQ ID NO: 6 (reference 1-4) and SEQ ID NO: 7 which encodes the human GRAIL of SEQ ID NO: 8 for producing said GRAIL protein. The GRAIL protein is approximately 50kD and migrates as a 3.75K mRNA on Northern. The specification further discloses the polynucleotide encoding GRAIL is used for expressing the GRAIL protein for identifying or detecting the expression of GRAIL in a biological specimen associated with T cell angery in vitro.

With the exception of the specific isolated nucleic acid molecule mentioned above, there is inadequate written description about the structure associated with function of *any* isolated nucleic acid molecule comprising *any* sequence encoding *any* Grail protein because the term "nucleic acid molecule" without SEQ ID NO has no structure, much less about the function of "GRAIL protein".

With regard to claim 2, SEQ ID NO: 7 is an isolated nucleic molecule encoding GRAIL protein comprising the amino acid sequence of SEQ ID NO: 8.

With regard to claims 3-5, the term "comprising" is open ended. It expands the "fragment" of SEQ ID NO: 7 such as 18 or 50 contiguous nucleotides to include additional nucleotide at either or both ends. There is inadequate written description about the fragment having additional undisclosed nucleotide.

With regard to isolated nucleic acid that "hybridizing under stringent conditions" as recited in claim 6, the claim encompasses any random nucleotide sequence of any length which hybridizes under undisclosed " stringent conditions" for the specific nucleic acid molecule that may or may not bind specifically to SEQ ID NO: 7 which encodes a "GRAIL protein". There is inadequate written description about the "stringent conditions" used for hybridizing to the specific polynucleotide of SEQ ID NO: 7. Although the specification on page 6 discloses a generic hibridization under stringent condition, the specific hybridization condition for the SEQ ID NO: 7 is not disclosed.

With regard to claims 7-10, since the isolated nucleic acid in claim 1 lacks structure associated with function, it follows the expression cassette comprising the undisclosed nucleic acid encoding any GRAIL protein under the transcriptional regulation, transcriptional initiation and termination is not adequately described. It also follows that the host cell comprising said expression cassette is not enabled, in turn, the method making the protein such as GRAIL is not adequately described. Further, the specification discloses only two polynucleotides such as SEQ

ID NO: 5 and 7 encoding human and murine GRAIL, respectively. Given the lack of a written description of any additional representative species of nucleotide encoding GRAIL, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.* Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,747,299 A (May 1998, PTO 892).

The '299 patent teaches an isolated nucleic acid other than a naturally occurring chromosome comprising a sequence encoding a protein from gene related to anergy in lymphocyte (GRAIL) such as cysteine string protein (See entire document, Summary of Invention, reference SEQ ID NO: 6, in particular). The '299 patent further teaches the reference nucleic acid can be used to prepare an expression cassette with the gene such as the transcriptional initiation and termination region that is functional in the host cell for expressing the reference protein (See column 6, lines 57-61, in particular). Claims 8 and 9 are included in this rejection because the cellular progeny of the reference cells transfected with the reference nucleotide for production of the reference protein inherently contains the reference protein in the cytoplasm. Thus, the reference teachings anticipate the claimed invention.

13. Claims 3-6 are rejected under 35 U.S.C. 102(a) as being anticipated by US Pat No. 5,989,549 (Nov 1999, PTO 892).

The '549 patent teaches an isolated nucleic acid molecule wherein said nucleic acid is a fragment of the claimed nucleic acid of SEQ ID NO: 7 (See nucleotide 7-83 of reference SEQ ID NO: 3, in particular). The reference fragment has 77 nucleotides identical to nucleotide 1 through 77 of the claimed SEQ ID NO: 7. The term "comprising" is open ended. It expands the claimed nucleic acid molecule to include additional nucleotides at either or both ends to read on the reference nucleic acid molecule. The '549 patent further teaches isolated nucleic acid such as primers and RNA that hybridize under various hybridization conditions such as 1.5 mM MgCl2, 1x buffer, 0.2 mM dNTP's, 10 μM of each primers, 1-5 U Tag polymerase, in a final volume of 50 μl. The conditions were 1 min at 95°C, 1 min at 60°C, 1 min, at 72 °C for 30 cycle, followed by a 5 min extension at 72°C (See column 5, lines 1-6, in particular) to the reference said nucleic acid that has 77 nucleotides identical to nucleotide 1 through 77 of the claimed SEQ ID NO: 7 (See nucleotide 7-83 of reference SEQ ID NO: 3, in particular). Thus, the reference teachings anticipate the claimed invention.

14. Claim 2 is free of prior art.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.

Patent Examiner

Technology Center 1600

November 4, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600